# CLINICAL PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS – A STUDY OF 50 CASES

*Dissertation submitted to*

**THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY**

*In partial fulfillment of the regulations*
*for the award of the degree of*

## M.D. BRANCH - I

## GENERAL MEDICINE


**GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL**

**THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY**

**CHENNAI, INDIA**

**MARCH 2008**

# CERTIFICATE

This is to certify that the dissertation titled **"CLINICAL PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS - A STUDY OF 50 CASES"** is the bonafide original work of **DR. R. ARUN PRAKAS,** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2008. The Period of study was from June 2006 to July 2007.

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# DECLARATION

I, **DR. R. ARUN PRAKAS,** solemnly declare that dissertation titled **"CLINICAL PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS – A STUDY OF 50 CASES"** is a bonafide record of work done by me in the Department of Internal Medicine, Government Stanley Medical College and Hospital during June 2006 to July 2007 under the guidance of **Prof. S. NATARAJAN, M.D.,** Professor and Head of Department of Medicine, Government Stanley Medical College and Hospital, Chennai.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, in partial fulfillment of the University regulations for the award of **M.D. Degree (Branch – I) in General Medicine – March 2008.**

Place : Chennai.

Date :

**(DR. R. ARUN PRAKAS)**

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# CONTENTS

# INTRODUCTION

Systemic Lupus Erythematosus is an autoimmune disease in which the cells organs tissues undergo damage by tissue binding antibodies. Annual incidence of Systemic Lupus Erythematosus(SLE) is 2.8 per 1,00,000 in United States and Europe. Estimates of total number with this disease ranges from 20 – 60 per 1,00,000. More than 80% are females. Male to Female ratio is equal in young and old. Highest incidence is between 20 – 50 years of age. The frequency of Systemic Lupus Erythematosus concordance in monozygotic twin is 25% and with 1-2% among dizygotic twins.

## AETIOLOGICAL FACTORS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

### Genetic Factors

- HLA, B8, $DR_2$ $DR_3$
- Inherited Complement deficiencies, C4, null allele

### Environmental Factors:

- UV Light
- Physical and Emotional stress
- Infections
- Female sex harmones

**Drugs**

Procainamide

Quinidine

Hydralazine

Methyldopa

Chlorpromazine

Isoniazid

**FREQUENCY OF CLINICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

| | **INDIAN DATA %** | **WESTERN DATA %** |
|---|---|---|
| **ARTHRITIS** | **72 – 92** | **86 – 94** |
| **ALOPECIA** | **52 – 80** | **50** |
| **SKIN RASH** | **74 – 90** | **60** |
| **PHOTOSENSITIVITY** | **10 – 62** | **33 – 62** |
| **MALAR RASH** | **37 – 76** | **72 – 90** |
| **ORAL ULCERS** | **41 – 61** | **30** |
| **FEVER** | **74 – 91** | **80** |
| **LYMPHADENOPATHY** | **24 – 47** | **50** |
| **NEUROPSYCHIATRY** | **19 – 63** | **20 – 45** |
| **RENAL** | **35 – 73** | **29 – 73** |
| **CARDIAC** | **10 – 29** | **20 – 30** |
| **PLEUROPULMONARY** | **9-54** | **36 – 57** |

## 1982 REVISED ACR CRITERIA FOR CLASSIFICATION OF SLE

1. Facial Erythema (Butterfly Rash)
2. Discoid Lupus
3. Photosensitivity
4. Oral ulcers (Painless)
5. Arthritis (Non Erosive and involving two or more joints)
6. Serositis (Pleuritis and Pericarditis)
7. Renal Disorders (Proteinuria > 0.5 gm/day or $3^+$ cellular Cast)
8. Neuropsychiatry
    a. Seizures (other causes ruled out) (or)
    b. Psychosis (Other causes ruled out)
9. Hematologic disorder
    a. Hemolytic anemia
    b. Leucopenia (< 4000/$mm^3$)
    c. Lymphopenia (< 1500/$mm^3$)
    d. Thrombocytopenia (10000/$mm^3$)
10. Immulonogic disorder
    a. Anti DNA antibody
    b. Anti Sm antibody
    c. Anti Phospholipid antibody
    d. Anti cardiolipid antibody
    e. Positive Lupus anticoagulant

11. Anti nuclear antibody

In the absence of other causes for ANA positivity, if four of these criteria are present, at any time during the course of diseases, a diagnosis of SLE can be made with 95% specificity and 75% sensitivity.

# AIM OF THE STUDY

1. To analyse the clinical spectrum of manifestations of Systemic Lupus Erythematosus (SLE) patients.
2. To analyse the initial presentation of Systemic Lupus Erythematosus (SLE).
3. To analyse cumulative presentation of SLE.
4. To study various system involvement.
5. To analyse the cause of death of SLE patients.
6. To correlate the clinical and laboratory investigations.
7. To compare my study with western data.

# REVIEW OF LITERATURE

## HISTORICAL REVIEW

The term Lupus is Latin for "Wolf". This term was attributed to 13th Century physician Rogerius[1].

The Frenchman Cazenave in 1851 was the first one to apply the term Lupus Erythematosus. Van Hehra, a Viennese Physician Latinized the disease in his text book "Atlas of skin diseases". In 1872[2] Moretz Kaposi recognized the visceral involvement. He proposed two types of disease.

1. The discoid 2. Disseminated form. He characterized the disseminated form by:

(a) Subcutaneous Nodule (b) Arthritis (c) Lympadenopathy (d) Fever (e) Weight loss (f) Anemia (g) Central Nervous system involvement.

In the 1920s and 1930s, SLE was identified as a distinct clinical entity, largely because of work of pathologists. An example of this was the atypical non bacterial endocarditis described by Emmanuel[3] Libmann and Benjamin Sacks in 1924.

The renal wire loop lesions and other findings were first described in 1934 by George Baecher. Friedberg, Gross and Wallache recognized

for first time that disease could occur with out skin manifestations. Hack and Reinhart were the first to describe the false positive syphilis test in SLE.

In 1948, Hargrares Richmond and Morton[4] described "LE Cell" in the marrow of SLE patients. In 1957, an American Physician George Frion, applied the indirect fluorescent techniques of Coons to study of auto antibodies[5]. At about the same time, Deicher, Holman and Kunkol[6] auto antibodies to DNA. Tann and Kunkel (1956) described anti SM antibody[7]. The recognition that SLE was familial was reported by Leonhardt in 1954 later studied by Shulman and Arnett at Hopkins[8].

**EPIDEMIOLOGY OF SLE**

Descriptive epidemiologist studies of SLE have been conducted worldwide. The more extensive data[9] are available from Scandinavia especially from Sweden and United States.

In the United States, blacks[10] have threefold higher incidence prevalence and mortality rates than do caucians.

Analytic and genetic epidemiology studies suggest a multifactorial aetiology of SLE, Polygenic mode of inheritance including role of an autosomal dominant auto immune gene, female sex hormones and clinical exposures.

## CLINICAL MANIFESTATIONS OF SLE

The diagnosis of SLE should be made principally on clinical grounds with support of laboratory tests.

The American College of Rheumatology has designated 11 criteria. Presence of (4) or more criteria is mandatory for the diagnosis.

## LATENT LUPUS[11]

Patients who fail to meet 4 of the 11 criteria are more appropriately called as "Lupus like Syndrome", incomplete or "Latent Lupus"

The clinical manifestations are protean. In order of frequency, they are as follows:-

## MUSCULOSKELETAL

The most common presenting symptom of SLE is arthritis.

### 1. ARTHRITIS

Usually episodic, oligoarticular[12], migratory; non erosive, non deforming and symmetrical arthropathy. Multiple joints are involved and 80 – 95% have tender swollen effusive joints. PIP/MCP/Knees and wrists are commonly involved. The most frequent musculoskeletal X ray[13] changes are soft tissue swelling/acralsclerosis and periarticular demineralization.

Lupus does not involve the spine. Joint fluid analysis typically shows reduced white cell count and more mononuclear cells.

**SYMMETRICAL ARTHRITIS SLE**

## 2. AVASCULAR NECROSIS

- 10 – 30% of patients with SLE can have this
- It is polyarticular in 90% of the bone
- AVN is more commonly found in hips/carpal bones of wrist/and humeral heads[14]
- 8% of cases are asymptomatic
- MRI is diagnostic though routine X ray can also be useful.

## 3. SEPTIC ARTHRITIS

- ❖ Should be suspected as a cause of Joint pain whenever there is swelling and warmth of a Joint coupled with peripheral leucocytosis.

- ❖ Aspiration of joint fluid and culture may be mandatory and life saving.

## 4. MYOSITIS

- Can present[15] in 3 – 5% of SLE patients.
- CPK is rarely elevated
- EMG can be abnormal
- Varying degrees of Lymphocytic/monocytic and plasma cell infiltration can be observed
- Muscle disease in SLE can also be secondary to corticosteroid therapy and antimalarials.

## SYSTEMIC

Systemic complaints like fever; weight loss and fatigue are often the initial complaint in 95% of patients. Among them fatigue[16] is the most common and is like chronic influenza. Weight loss is mostly due to malabsorbtion of overlap illness or anorexia of severely debilitated

patients with CRF or liver disease and is not due to SLE perse. Fever[17] is of low-grade type and rarely exceeds 102ºF. A temperature of more than 102 ºF needs infection to be ruled out.

## SKIN MANIFESTATIONS

The skin lesions in SLE are classified in to those that are Lupus specific histologically and those that are Lupus non specific[18]. The lupus specific lesions are divided into Acute sub acute and chronic.

## LUPUS SPECIFIC LESION

### Acute Lesions

The most recognized skin manifestation of SLE is butterfly rash, which usually presents acutely as an Erythematus, elevated lesion, pruritus painful in a malar distribution, commonly precipitated by exposure to sunlight. The rash lasts, from days-weeks. Its presence facilitates the diagnosis of SLE and is commonly accompanied by other inflammatory manifestations of disease. By immuno florescence, the classic immune deposits at dermal epidermal junction may be seen. The presence of immune deposits in uninvolved skin in patients with SLE has been believed to be helpful in diagnosis.[19]

Other acute cutaneous lesions are generalized erythema and bullous lesions.

**ACUTE LE LESION + ORAL ULCER**

## SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (SCLE)

SCLE refer to a distinct cutaneous lesion that is non fixed, non scarring exacerbating and remitting. This lesion is intermediate between evanescent malar rash of active lupus and chronic lesion of disease which usually cause scarring. These lesions generally occur in sun-exposed areas and may be generalized. The lesion originate as Erythematus papule or small plaques with a slight scale, and may evolve further to a plaques and scale the papulosquamous variant, which mimics psoriasis or lichenplanus or merge and form polycyclic or annular lesions.

**SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS**

**SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS**

**SLE SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS**

**Photo sensitivity**

More than 50% of patients with SLE demonstrate photosensitivity. In addition to skin lesion, patients may develop exacerbation of systemic disease. The mechanism of photosensitivity is unknown, but it has been suggested that lymphocyte from patients with SLE are sensitive to 360 – 400 nm light related to clastogenic factor in these cells.[20]

**SLE MALAR RASH**

**SLE ALOPECIA**

**SLE LICHEN PLANUS**

## CHRONIC LESIONS IN LUPUS

Discoid lesions are chronic cutaneous lesions that may occur in absence of any systemic manifestations, as discoid lupus or may be manifestation of SLE. These lesions often begin as erythematous papules. With scaling that may become thick and adherent with a hypo pigmented central area. As lesions progresses, follicular plugging occurs. With development of scarring with central atrophy. Discoid lesions occur in malar area or sun exposed areas. Lesion in scalp lead to extensive permanent alopecia. Discoid lesion may be localized or generalized. Generalized discoid lesion A/W systemic features and serological abnormalities.

## RENAL SYSTEM

Renal involvement is found in ½ to 2/3 of patients with SLE.[21] It is due to deposition of immune complexes in the mesangium or sub epithelial, sub endothelial regions of glomeruli.

## WHO CLASSIFICATION OF LUPUS NEPHRITIS

| Class | Pattern | Site of immune complex deposition |
|---|---|---|
| I | Normal | None |
| II | Mesangial | Mesangial only |
| III | Focal and segmental proliferative | Mesangaial, Sub endothelial ± Sub epithelial |
| IV | Diffuse proliferative | Mesangial, Sub endothelial, Sub epithelial |
| V | Membranaous | Mesangial, Sub epithelial |

Both diffuse proliferative[22] GN and progressive forms of focal proliferative Nephritis have poor prognosis. Membranous nephropathy; sclerotic glomeruli, fibrous crescents tubular atrophy; and interstitial fibrosis denotes inactive lesion. Renal involvement can be assessed by 24 hours urinary protein excretion > 500 mg; Creatinine clearance; complete urine examination with urinary cytology to detect the presence of RBC/WBC/Hyaline and granules casts in urine called as "Telescoped Urine"[23] which is indicative of severe nephritis. Urine cytology score

2.0 - without disease

6.8 - Mild activity

11.0 - Moderate – severe activity

**LUPUS NEPHRITIS**

The incidence of Lupus Nephritis is higher in male patients.[24] The classification of Lupus Nephritis is primarily histological. Renal biopsy is useful in planning current and near future therapies. Diffuse proliferative glomerulo nephritis is more common in male compared to female.[25] The presence of anti DNA antibodies and decrease of $C_3$ were statistically associated with kidney disease.[26] If diffuse proliferative glomerulo nephritis is untreated all patients develop ESRD in 7 years. Therefore, aggressive immunosupression is indicated unless damage is irreversible. The proportion of male with severe lupus nephritis presenting with hypertension and reduced Creatinine clearance massive

proteinuria and reduced level of complement leading to end stage renal disease was significantly higher compared to females. Thus, lupus nephritis in male is a progressive and severe in comparison to female.[25]

## CARDIOVASCULAR LUPUS

Patients with SLE may present with following cardiovascular manifestations.[26,27] in decreasing order of frequency; Pericarditis 12 – 47%; LV dysfuction 4 – 71%; Myocarditis 5 – 10%; valvular disease; conduction disturbance 10%; pulmonary hypertension 2 – 9%; systemic hypertension 15 – 56%, Coronary atherosclerosis 7 – 9%.

## PERICARDITIS

Occurs in 12 – 47% of living SLE patients; autopsy studies much higher prevalence of pericardial involvement ranging up to 61 – 100%. It is the most common manifestation and may be the first manifestation.

### i. PLEURO PERICARDIAC[27]

Pain may be first symptom constrictive Pericarditis and cardiac tamponade are rare. Diagnosis was based on presence of pericardial friction rub in 71% diagnostic ECG changes in 33% and evidence of pericardial effusion by echo in 50%. Pericardial fluid is exudative; anti DNA low complement may be demonstrated in pericardial fluid.

## ii. LV DYSFUNCTION

Echo cardiographic studies show 4 – 71% of SLE patients have some degree of LV dysfunction patient may present with gallop rhythm new murmur on CCF, X ray chest shows cardiomegaly. Diagnosis is made Echo.[28]

## iii. MYOCARDITIS

The clinical recognition of Myocarditis ranges from 3 – 15% . Most of time sub clinical. Patient may present with CCF (or) Tachycardia (or) Dyspnea. Myocarditis should be considered in patients with Tachycardia, third heart sound, abnormal ECG those with new murmurs, conduction disturbance and in those with CCF. Diagnosis is confirmed by global hypokinesia on Echo confirmed by right ventricular endomyocardial biopsy. Immunofluorescence study of endomyocardial biopsy show Perivascular deposits of IgG and vascular deposits of C3. More recently Ga 67 citrate scintigraphy.[29] useful in detection of SLE Myocarditis. Another method is Indium[33]III antimyosin Fab imaging for detection of myocardial involvement.

## iv. VALVULAR HEART DISEASE

Occurs[31] in 25 – 93% of SLE patients mitral and aortic regurgitations are the most common. Stenotic lesions very rare. Libmansacks[32] described that verrucous endocarditis can affect valve leaflets, papillary muscles and mural endocardium. These valvular

vegetations do not involve the line of closure and should not deform the valve. Shearn found that systolic murmurs occurred in 70% of SLE patients. Only 4% of SLE patients can have diastolic murmur. Trans Oesophageal echo cardiogram is modality of choice to detect valvular heart disease in SLE.

### v. CONDUCTION DISTURBANCES[34]

Approximately 10% adult SLE patients can have conduction disturbances. Sinus Tachycardia is seen in 61 – 100% of patients. Arrythmias are found more commonly in SLE patients with Pericarditis and Myocarditis.

### vi. CORONARY ARTERITIS

Rare in SLE. Angina and myocardial infarction are most common clinical presentation. Serial coronary angiography helpful in diagnosis.

### vii. PULMONARY HYPERTENSION[42]

It is unusual in SLE patients unlike in MTCD and scleroderma. Various studies show the cumulative frequency of above 2 – 9% Pulmonary Hypertension in SLE patients. It is usually asymptomatic and discovered on a screening echo Doppler. Right heart catheterization is reserved for symptomatic patients and to guide therapy. Ventilation – perfusion scanning is done to rule out the possibility of multiple pulmonary emboli. Primary pulmonary Hypertension occurs in patients

of SLE with Raynaud's phenomenon. Other mechanisms being pulmonary vasculitis antiphospholipid antibody syndrome and interstitial lung disease.

## viii. SYSTEMIC HYPERTENSION

Prevalence of systemic hypertension in SLE patients is from 15 – 56% in various studies. All patients with hypertension in the series of Arms Cruz et al and 86% of those in Estes and Christina series had lupus nephritis. Budman and Steinberg found that systemic hypertension in SLE patients in absence of renal disease was associated with usage of corticosteroids. Systemic Hypertension is one of the strongest predictors of preterm birth in Lupus pregnancy.

## ix. CORONARY ATHEROSCLEROSIS IN SLE

Prospective studies show clinical detection of angina and myocardial infarction is seen with 7 – 9% of SLE patients. Cross sectional (or) Retrospective studies show exercise induced ischemia in 11-23% of SLE patients. Patients usually present in their early 40's with angina; myocardial infarction (or) sudden death. Coronary angiography is the gold standard investigation for this. Stress ECG lack both sensitivity and specificity. Rest and perfusion myocardial single photo emission CT (SPECT) is one of the most sensitive and specific means of assessing the presence of atherosclerosis but are expensive. Magnetic resonance angiography can be used.

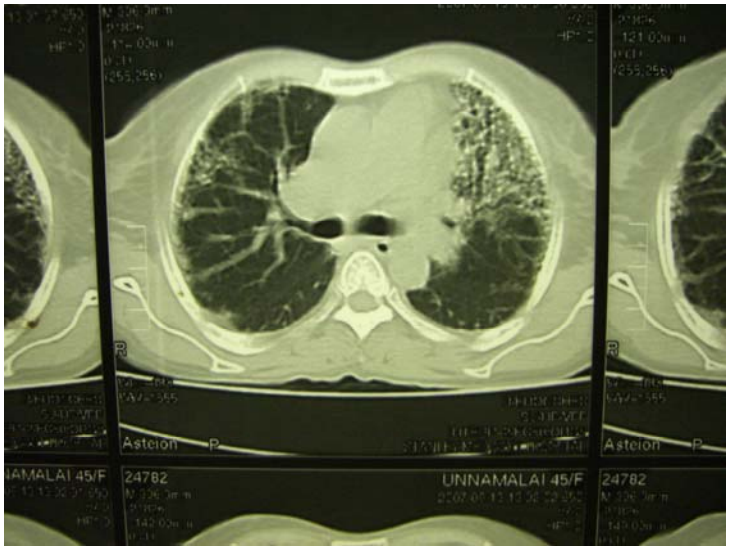
## GASTROINTESTINAL TRACT / SLE

Occurrence of painless ulcers in the nose and mouth is m/c c/f of GIT lupus. Almost 100% of patients develop these at some time in the course of their disease. These ulcer indicate a flare. Nausea/vomiting is found in 30%. Abdominal pain in SLE patients can result from pancreatitis. Ischemic bowel; perforation (or) mesenteric vascultis.[38] and intussusception. Lupus peritonitis [39] is the result of small vessel involvement in the bowel serosa/retro peritoneum or due to actual perforation of the bowel bacterial peritonitis is quite common in patients with Nephrotic syndrome. Parenchymal liver disease[40] is quite uncommon but liver function studies may be abnormal secondary to drug therapy. Aspirin ingestion[41] and rarely with thrombosis secondary to Phospholipid syndrome.

**SLE ORAL ULCER**

## PULMONARY DISEASE AND LUPUS[43]

Over 50% of SLE patients can have some form of pleural disease in their lifetime. Simple Pleuritis is the most presentation than exudative pleural effusion. Parenchymal lung involvement can occur less commonly and may present as acute pneumonitis with dyspnoea. Pleuritic chest pain hypoxemia and patchy infiltrations. The most common cause of pulmonary infiltrate in SLE patients is infection[44]. Hemoptysis and overt pulmonary hemorrhage[45] are emergencies in SLE patients and can be result of pneumonitis (or) pulmonary hemorrhage. Shrinking lung found in X-ray chest in some SLE patients is result of recurrent atelectasis and diaphragmatic weakness[46]. The most common pulmonary function abnormality in lupus is reduced carbon monoxide diffusion capacity[43].



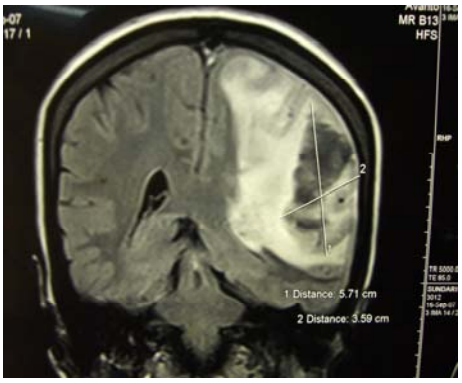

## INTERSTITIAL LUNG DISEASE

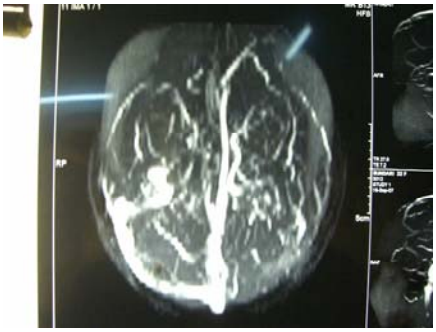
## CENTRAL NERVOUS SYSTEM

66% of SLE patients manifest neuropsychiatry features[35]. Pathogenesis being thrombosis, vasculitis and non immunogenic in nature. C/F include seizure, psychiatry illness, cranial nerve involvement, CVA and peripheral nervous system involvement.

### i. SEIZURES

It is found in 15 – 20 % of SLE patients. GTCS is the most common form though other types have been reported lupus vasculitis, thrombosis, steroid therapy: a concominant metabolic problem like Uraemia account for the cause.

## ii. PSYCHIATRY MANIFESTATIONS[36]

50 – 67% of patients with SLE manifest this. Overt Psychosis is seen in 12% of SLE patients. Usually presents as severe depression and sleep disturbance. Anti ribosomal 'P' proteins are present in over 60% of patients with SLE related. Psychosis and can help distinguish these patients from steroid psychosis[37].

## iii. CRANIAL NERVE INVOLVEMENT

Occur in 10% of SLE patient. It may be presenting symptom in small number of patients.

## iv. C V A

Risk of CVA is more during first five year of disease. The incidence is 6.6% during first year.

## v. PERIPHERAL N. SYSTEM

Peripheral N. System is seen in 3.15% patients of SLE. It present as:

a. Sensory
b. Sensory Motor Neuropathy
c. GBS
d. Mono neuropathy
e. Mono neuritis multiplex

Spinal fluid pleocytosis and high spinal fluid protein levels (or) both are helpful indication oligoclonal bands are seen in SLE CSF.

CT Brain: MRI, PET scanning can detect infarct and demyelinating diseases.

**SLE VASCULITIS**

**SLE VASCULITIS WITH FOOT DROP**

## HEMATOLOGY OF SLE[47]

The cellular elements[48] of blood and coagulation pathway can be affected in SLE. Anemia occurs in 60 – 70% of patient as anemia of chronic disease. Other types like autoimmune hemolytic anemia is found in <10% patients. Positive coomb's Test can be found in 20 – 60%. Leucopenia of either granulocytopenia (or) Lymphopenia can be found in 50% SLE patients. Antibodies directed against the cellular elements at any point in their maturation pathway is the cause of it. Immuno suppressive treatment reverse the cytopenias. Thrombocytopenia is found in 30 – 50% of SLE patients and is related to either anti platelet antibodies/antiphospholipid antibody. Platelet count can be used as a parameter to assess the response to treatment. Anti clotting factor antibodies that are directed most commonly to factor 2, 7, 9, xi and xii. Lupus anticoagulants that are associated with mild profoundly raised PTT are also found in SLE. The hypercoagulable state in Lupus patients can be due to variety of reasons like present of procoagulant antibodies, hereditary deficiency of factor C, S and antithrombin 3.

**SECONDARY APLS / D.V.T.**

## HEMOTOLOGICAL MALIGNANCY[49]

There are reports that concern with a viral related etiology such as liver and vulval carcinoma are found in excess. Patient with SLE have ↑ risk of Nonhodgkins lymphoma[49].

## EYE/SLE

Eye is not commonly involved. Episcleritis[50]. Conjuctivitis are found in only 10%. Iritis optic neuritis papilledma and retinal vein occlusion are major problems. Lupus retinopathy[51,52] is common in patients with active SLE and those with lupus cerebritis. Retinopathy includes micro aneurysm, cotton wool spots, papilledema and retinal vasculitis.

## PREGNANCY[53] AND SLE

Pregnancy has varied effect on SLE activity. Fertility rates are normal in SLE but spontaneous abortions and still birth are frequent (10-30%) in patients with LA/ACL. Disease flare especially during 6th week postpartum. There is increase in pregnancy complications like toxemia neonatal lupus IUGR heart block abortion and premature delivery are hazard to foetus. Most patients deliver normal infants is cardiac and renal disease is absent and SLE activity is controlled. Glucocorticoids like dexamethasone and betamethasone which are not inactivated by placental enzymes must be used to suppress disease activity. Neonatal lupus consist of transient skin rashes and permanent heart block and is due to transmission of maternal anti RO across the placenta.

## LABORATORY EVALUATION[55] OF SLE:

The laboratory assist the clinician to:

1. Obtain additional criteria that complement the history and physical examination.

2. To assess the extent of organ involvement

3. To obtain a quantifiable parameter to follow evolution of disease.

## INITIAL TEST

Complete blood count, blood biochemistry, ESR, CRP, Urine Analysis.

## CBC

- Anemia of normochromic normocytic occasionally hemolytic type
- Leukopenia Lymphopenia, Thrombocytopenia.

## BLOOD BIOCHEMISTRY

Serum Creatinine, blood urea, Creatinine clearance to know about renal deterioration.

## ESR

Rise in ESR correlates with disease activity in the absence of infection. Most patients even with quiescent disease have westergren ESR of upto 70 mm/hr Higher values > 100 denotes vasculitis and infection.

## CRP

Persistent mild rise in CRP occurs in SLE with Jaccound's arthropathy. High CRP > 60 mg/dl is seen in SLE patients during inter current infections and in lupus associated Serositis.

## URINE ANALYSIS

Urine for 24 hrs protein estimation > 500 mg/24 hrs.

- ❖ Proteinuria = active disease
- ❖ Urine cytology for hyalin[56]granular/RBC/WBC casts = severe nephritis

## SPECIFIC TESTS

## ANA

These tests are best screening tests. Indirect immuno fluorescent assay is the gold standard method. If the test substrate contains human nuclei WIL.2 (or) HEP-2 cells[57] more than 95% of Lupus patients will be positive. These test have high sensitivity (97 – 100%) but low specificity and predictive value of 10 – 40%. A positive ANA test is not specific for SLE. It can occur in some normal individuals in low titre with aging other autoimmune diseases, viral infections. Chronic inflammatory processes and by several drugs. So positive ANA test supports diagnosis of SLE but not specific. A negative test makes the diagnosis unlikely but not impossible. Antibodies to (ds DNA) and to Sm done by fair assay are relatively specific for SLE. Determination of complete antibody profile of each patient helps product clinical subsets.

## COMPLEMENT STUDIES

Total functional hemolytic complement (CH50) levels are the most sensitive measure of complement activation but subjected to lab error. Very low levels of CH50 with normal levels of $C_3$ suggest inherited deficiency of a compliment component which is highly associated with SLE and with ANA negativity. The CH50 assay is a functional assay but can be normal even when one (or) more components are low. $C_3/C_4$ are the most widely available but are not functional assays. CH50 and $C_4$ tends to fall early before clinical signs of disease activity occurs, where as $C_3$ often continues to decline during the height of clinical illness. In patients with active nephritis (or) vasculitis fall in $C_4$ levels are often markedly depress than $C_3$. Normal $C_3$ is more predictive of inactive renal disease. As with anti ds DNA the association of complement levels and disease activity. Varies from patient and has to be assessed on an individual basis.

## ANA NEGATIVE SLE[58]

The original papers of Gladman et al. Fessel and Maddison et al, drew specific attention to the subset of patient with ANA negative lupus. This subset is negative for the usual screening test used to diagnose SLE but displayed other clinical serological manifestations characteristic of disease. Possible reasons could be laboratory error, prozone phenomenon and hidden ANA in the serum.

## FREQUENCY OF VARIOUS ANTIBODIES IN SLE:

| Autoantibody specificity | Frequency % |
|---|---|
| Native (Double standard) DNA | 40.75% |
| Denaturanted simple standard DNA | 60 – 90 |
| Sm | 15 – 35 |
| Nuclear RNP | 30 – 85 |
| SSA | 27 – 60 |
| SSB | 8-50 |
| Histone (total) | 50-90 |
| Ribosomal RNP (P protein) | 12-16 |

## LE CELL TEST[14]

In LE cell test, the patients serum is incubated with normal WBCs. If the LE factor, an antibody to whole nucleoprotein is present in patients serum it penetrates in to nuclei of some of the normal WBCs and causes nuclear damage. The damaged Nuclei being Leucotactic are then phagocytosized by some of neutrophils that have escaped damage. If a smear of incubated WBCs is made and stained with Wright stain, the phagocytosized nuclear material may be observed within some of neutrophils as large round, amorphous, smoky basophlic body of such large size that it presses the nucleus of a neutrophils against cell membrane. This represents LE cell.

## LAB MONITORING OF DISEASE ACTIVITY:

Hematological manifestations as indicators of Disease activity.

Hemolytic Anemia +

Leucocytopenia +

Thrombocytopenia +

Renal parameters as indicators of disease activity

Hematuria +

Polyuria +

Cast (WBC, RBC, Tubular) +

Proteinuria +

- For monitoring SLE, activity the urinary sediment is more useful than creatinine clearance.

- Creatinine clearance is more useful than Creatinine alone.

## AUTO ANTIBODIES

Antibodies to ds DNA are useful in assessing disease activity. The association is stronger in nephritis flares than in normal exacerbations. Several prospective studies demonstrated increasing anti ds DNA titres preceeding clinical flares in 50 – 100% of cases but another study did not.

## IMMUNE COMPLEXES

Immune complex assays like PEG assay, Raji-cell assay, CIQ binding, anti $C_3$ and conglutinin are not well standardized and they are still largely investigational.

## COMPLEMENT STUDIES

CH50/$C_4$ tends to decrease early before clinical signs of disease activity occur. $C_3$ often continues, to decline during the height of clinical illness. $C_4$ is markedly decreased than $C_3$ in active nephritis and vasculitis. Normal $C_3$ levels are predictive of inactive renal disease.

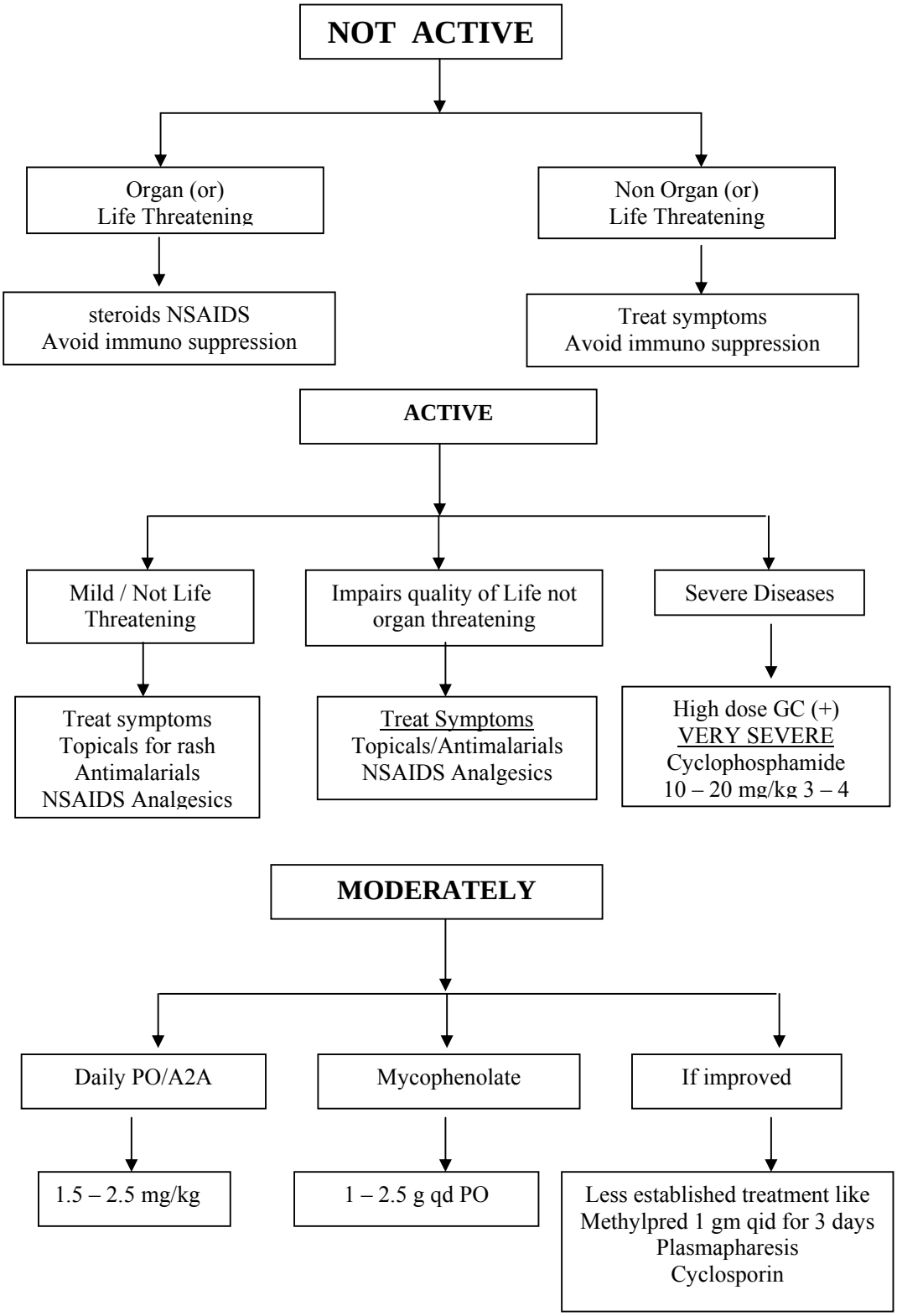
### Acute phase reactants

**ESR very sensitive but non-specific measure of**

1. Disease activity – elevation in absence of infection denotes disease activity.

2. CRP – mild persistent increase occurs in SLE with Jaccoud's arthritis. Increase more than 60 is seen in intercurrent infections and lupus associated serositis.

## ALGORITHM FOR THE TREATMENT OF SLE DETERMINE ACTIVITY AND SEVERITY OF DISEASES



# MATERIALS AND METHODS

This study way conducted in 50 patients of Systemic Lupus Erythematosus who were attending Rheumatology Department, Medicine Department and Nephrology Department, Stanley Medical College Hospital during the period from June 2006 – July 2007.

All the patients of Systemic Lupus Erythematosus who presented with varying signs and symptoms included in this study and were analysed clinically and laboratory wise.

A detailed history was taken with particular emphasis on various organ system involvement.

**Symptoms included:**

Constitutional - Fever; Malaise; Fatigue; Weight loss

Musculoskeletal - Pain; Swelling of joints

Mucocutaneous - Rash; Photo sensitivity; Pruritus

Cardio vascular - Chest pain; dyspnea; palpitations; syncope

CNS - Seizures; hallucinations; Abnormal behaviour;

symptoms of peripheral neuropathy

Renal - Hematuria

GIT - Oral Ulcer; acute abdominal pain; abdominal Distension; foetal wastage

This was followed by detailed clinical examination. The following in general examination.

- Photo sensitivity; Malar rash; Discoid Lupus Erythematosus (DLE); Purpura; Urticaria; Erythema; Raynaud's phenomina
- Arthritis; AVN; Osteoporosis
- Pericardial rub; Pleural Rub; Cardiac murmurs
- Anemia; Petechiae; Lymphadenopathy

An elaborate laboratory examination was done which include albumin deposits cellular carsts haemoglobin casts, tubular casts and urine 24 hrs urinary protein more than 500 mg/dl, Serum Creatinine VDRL CRP $C_3$ $C_4$ Antinuclear antibody. X ray chest, ECG, Echo, USG Abdomen, Renal biopsy and skin biopsy in selected patients.

For microscopic examination of urine, a clean catch early morning $2^{nd}$ voided midstream. Urine sample while patient was still fasting were collected and examined in 1 – 3 hrs to avoid lysis of cell and casts and to ensure a reasonably concentrated and acidic urine specimen larger than concentrated volume of urine of about 50 ml.

Dysmorphic erythrocyte indicate injlamatory glomerular or tubule interstitial disease while monomorphic RBC's indicate lower urinary tract bleeding.

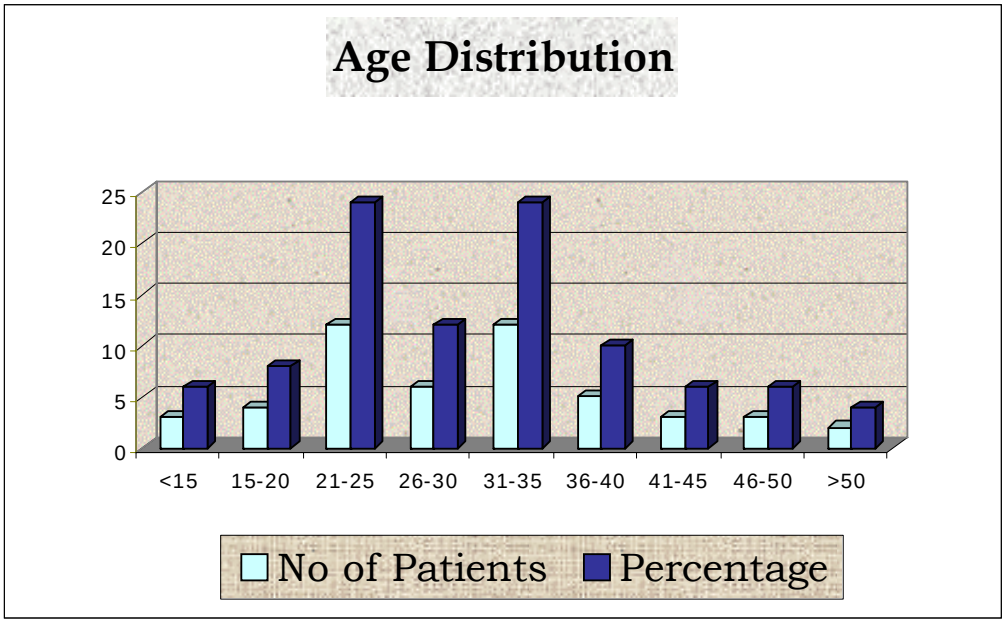
A telescopic urine sediment contains full range of cell and casts it indicates global nephron involvement.

# OBSERVATION RESULTS

## AGE DISTRIBUTION IN THIS STUDY

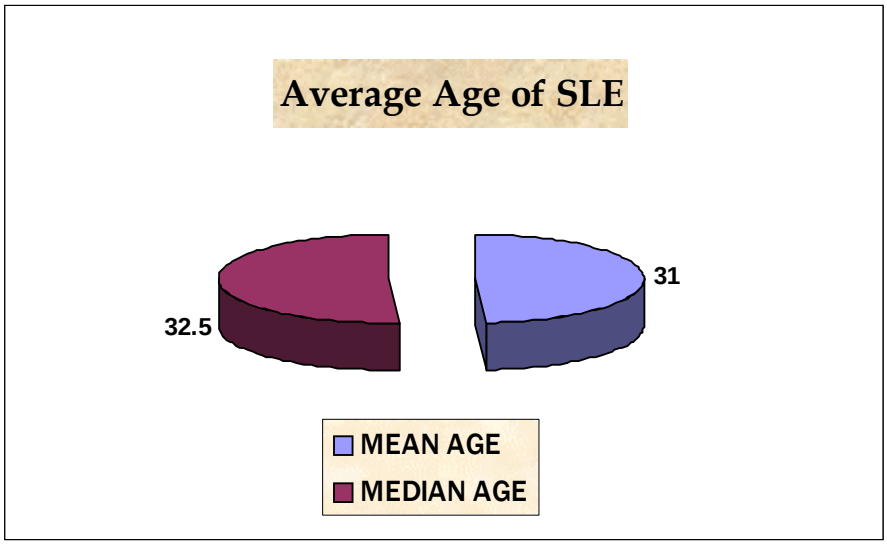
### NO. OF PATIENTS = 50

| AGE IN YEARS | No. of patients (50) | Percentage (%) |
|---|---|---|
| < 15 | 3 | 6% |
| 15 – 20 | 2 | 4% |
| 21 – 25 | 13 | 26% |
| 26 – 30 | 5 | 10% |
| 31 – 35 | 15 | 30% |
| 36 – 40 | 3 | 6% |
| 41 – 45 | 3 | 6% |
| 46 – 50 | 3 | 6% |
| > 50 | 2 | 4% |



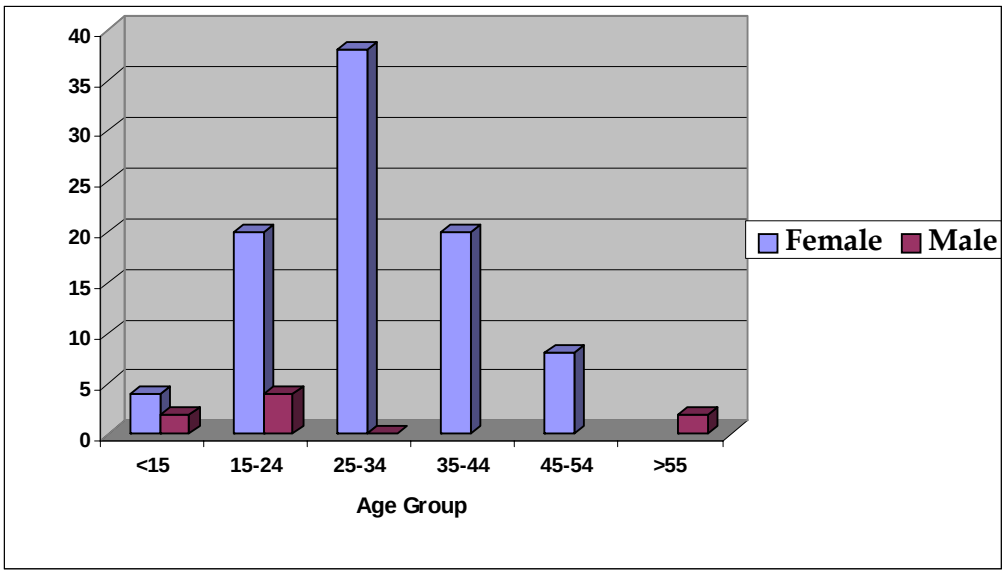
## AVERAGE AGE OF SLE

| | |
|---|---|
| MEAN AGE | 31 |
| MEDIAN AGE | 32.5 |



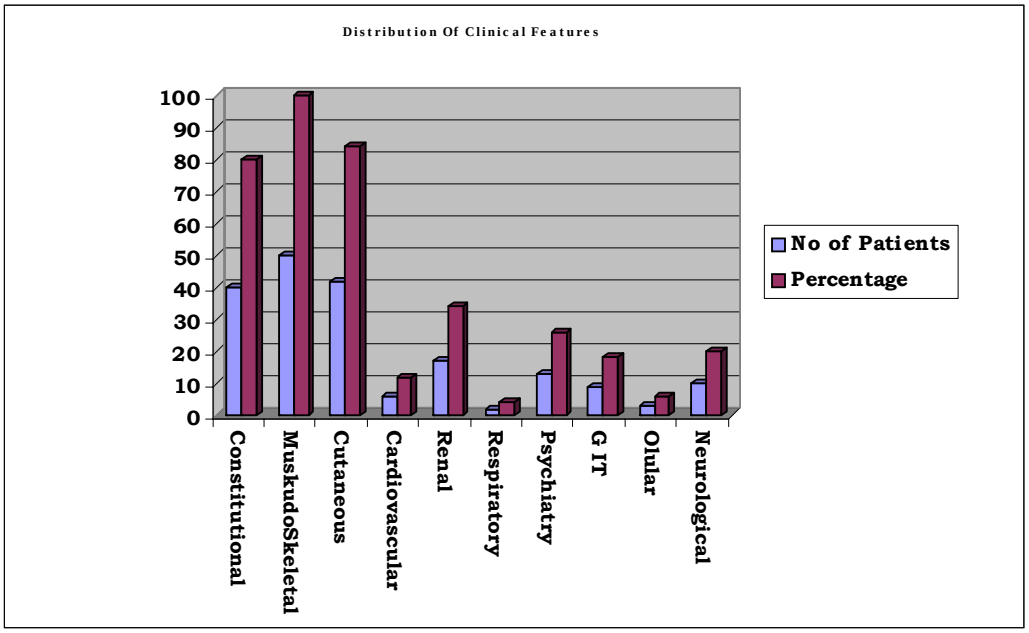
## AGE DISTRIBUTION IN MALE / FEMALE

| Age Group | Female | Male |
|---|---|---|
| < 15 | 4 | 2 |
| 15 – 24 | 20 | 4 |
| 25 – 34 | 38 | 0 |
| 35 – 44 | 20 | - |
| 45 – 54 | 8 | - |
| > 55 | - | 2 |



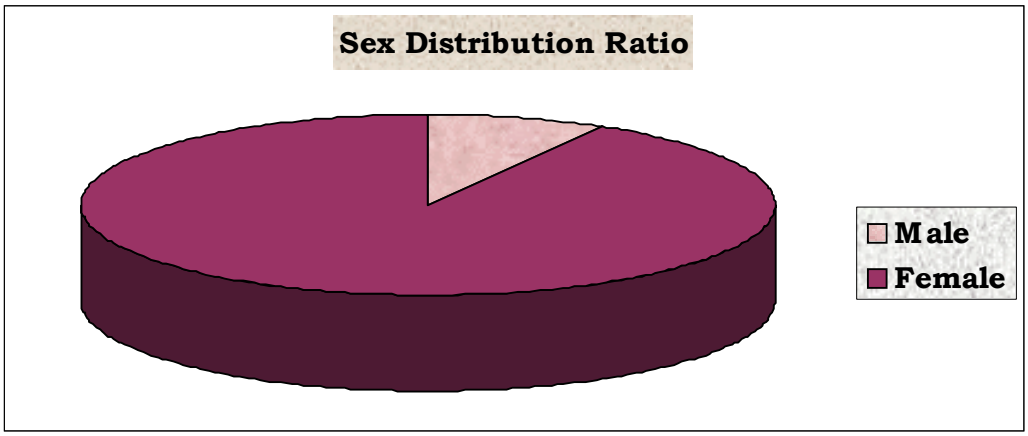
## DISTRIBUTION OF CLINICAL FEATURES

| Clinical Presentation | No. of Patients | Percentage |
|---|---|---|
| Constitutional | 40 | 80 |
| Musculoskeletal | 50 | 100 |
| Cutaneous | 42 | 84 |
| Cardiovascular | 6 | 12 |
| Renal | 17 | 34 |
| Respiratory | 12 | 24 |
| Psychiatry | 20 | 40 |
| G IT | 24 | 48 |
| Ocular | 3 | 6 |
| Neurological | 7 | 14 |



## SEX DISTRIBUTION RATIO

| | |
|---|---|
| MALE | 1 |
| FEMALE | 9 |



# DISCUSSION

## INTERPRETATION OF CLINICAL MANIFESTATION

The study group contains 45 females and 5 males in the ratio of female to male 9:1.

Age of patient in the study varied from 14-60 years.

Mean Age is 31years.

Highest incidence is found in the age group of 29-35 years of age.

## INITIAL PRESENTATION OF SLE

At its onset SLE may involve one (or) more organ system. Overtime-additional manifestation of disease may occur.

## POLYARTHRALGIA

Among 50 patients, 29 had initial presentation of muskulo skeletal system in form of arthritis myositis and arthralgia. Thus arthritis and arthralgia are the m/c initial manifestation in our study. During course of disease almost all patients develop arthralgia.

## SKIN MANIFESTATION:

Skin manifestation as initial presentation is seen in 16 patients. Most common are photosensitive and malar rash seen over cheeks and

nose presented in 9 patients. 3 patients presented initially with discoid lupus erythematous. Thus skin manifestation is the second most initial presentation seen in our study.

**RENAL MANIFESTATION**

Among 50 patients, 5 patients presented initially with EDEMA of legs and Anasarca. Their 24 hr urine is in the Nephritic range. They are found to be lupus Nephritis on Renal biopsy. In STUDY OF ESTES and Christian study, Nephritis was initial presentation in 6% of cases.

**HAEMATOLOGICAL MANIFESTATION**

Hematological manifestation as initial presentation seen in 3 Persons. 2 patients presented with Cytopenia and fever. One patient presented initially in form of Idiopathie thrombocytopenia. Anemis and Thrombocytopenia were the initial manifestation in Christian and estes et al studies is 2%.

**NEUROPSYCIATRY MANIFESTATION**:

Among 50 patients, 6 patients presented with neuropsyciatry manifestation.Seizures are the presenting manifestation in 2 patients .one patient presented initially with young stroke who turned out to be SLE vasculitis.Post parum seizure as a initial manifestation is seen in our patient in $8^{th}$ postnatal life. She is ANA positive and Antiphospholipid antibody positive.

Thus in our study, most common initial manifestation is arthralgia. Percentage frequency of presenting clinical features in our study is compared to similar study from other parts of India [60].

| Manifestation | Northern | Southern | Eastern | Our Study |
|---|---|---|---|---|
| Arthritis | 57 | 86 | 75 | 58 |
| Skin lesions | 36 | 48 | 50 | 32 |
| Nephritis | 8 | 7.4 | 49 | 10 |
| Neuropsychiatry | 12 | 35 | 30 | 12 |
| Thrombocytopenia | 4 | 1.5 | N.A | 2 |

Initial presentation of our study is compared to Similar Study from western countries [61].

| | Our Study | Toronto | Europe |
|---|---|---|---|
| Musculoskeletal | 58 | 42 | 69 |
| Skin lesion | 32 | 66 | 40 |
| Neuropsychiatry | 12 | 20 | 12 |
| Renal lesion | 10 | 42 | 60 |

Western data shows higher incidence of renal lesions as initial manifestation compared to our study.

**CUMULATIVE PRESENTATION OF SLE**

Of 50 patients, 40 patients manifested one of constitutional symptoms like fever, malaise, and weight loss

Among 50 patients, 23 patients presented initially with muskuloskeletal symptoms like polyarthritis myositis muscle weakness. During course of time polyarthritis is seen in 45 patients and polyarthralgia is seen in all patients.

In a study of Hochberg et al, the occurance of muskuloskeletal involvement was 83%: of them 76% showed arthritis and 5% showed myositis.

The clinical feature in our study is compared to similar study in other parts of India. Study should m\c clinical manifestation in southern and northern India is polyarthritis.

**CUTANEOUS MANIFESTATION**

As far as cutaneous manifestation are concerned 41 patients should following manifestation.

| Manifestation | No of Patients | Percentage |
|---|---|---|
| Malar Rash | 21 | 42 |
| Photosensitivity | 36 | 72 |
| Alopecia | 46 | 92 |
| Discoid Rash | 6 | 12 |

Comparison of my study to Estes at el and Hochberg et al is as follows.

| Manifestation | Our Study | Estesetal | Hochberg |
|---|---|---|---|
| Cutaneous | 82 | 88 | 81 |
| M.Rash | 44 | 39 | 61 |
| Photosensitivity | 72 | - | 45 |
| Alopecia | 92 | 37 | 45 |
| Discoid Rash | 12 | 19 | 15 |

Compared with western data, the incidence of Alopecia and photosensitivity are more common.

The comparison of my study to similar study to other parts of India.[60]

| Manifestation | N | S | W | E | Our Study |
|---|---|---|---|---|---|
| Photosensitivity | 67 | 52 | 24 | NA | 72 |
| Alopecia | 82 | 75 | 53 | 70 | 92 |
| Skin lesion | 85 | 74 | 81 | 90 | 60 |

**RENAL INVOLVEMENT**

In our study 17 patients showed evidence of renal involvement.

Renal involvement as initial presentation is seen in 5 patients. They presented as gen anasarca and their 24 hr urine protein is in the nephritic range. They are found to be lupus nephritis on renal biopsy.

In our study 15 years old boy intialy presented as cytopenia, During course of time he developed polyarthralgia Alopecia and gen. Anasarca . His 24 hr urine protein is in nephritic range and renal biopsy shows diffuse proliferative G.N.

One patient presented initially with haematuria and red cell cast. During course of time she developed lupus nephritis. Renal biopsy reported as class 2 nephritis. Renal Biopsy was done in 17 patients and was found that D.P.G.N [class 4] Nephritis is most common histology seen in 7 patients.

2 patients showed class 2 Nephritis; 2 patients showed class 3 Nephritis: 2 patients have normal biopsy and 4 patients showed class [5] Membranous Nephritis.

In male lupus diffuse proliferative glomerulo nephritis is the most common histology [63].

Regarding respiratory system involvement 12 patients showed pulmonary manifestation in form of PLEURAL Effusion [B/L] (or) unilateral in 6 patients [12%]. Intertitial pneumonitis in 1 patient [2%] and pneumonic consolidation in 5 patients [10%].

In Estes et al study occurrence of lupus pneumonitis was 9% fibrosis was 6%.

About 6 patients showed evidence of cardiovascular involvement. 5 of them presented with valvular abnormality with mild pulmonary hypertension. One patient had Libman Sac Endocarditis.

**CNS Manifestation**

About 27 patients [54%] showed evidence of CNS involvement in the form of seizure 4 patients [8%]; peripheral motor neuropathy 2 patients [4%]; young stroke in 1 patients [2%] and neuropsychiatry manifestation in the form of insomnia and depression in 21 patients. Headache is presented in 19 patients.

The comparative study of neuropsychiatry manifestation in this study to estes et al and Hochberg et al as follows.

| Manifestation | Our Study | Estes et al | Hochberg et al |
|---|---|---|---|
| CNS | 54% | 59 | 55 |
| GTCS | 8% | 13 | 26 |
| Peripheral Neuropathy | 4% | 7 | 21 |
| Stroke | 2% | - | 5 |
| Neuropsychiatry | 42% | 37 | 16 |

Vasculitis lesion at tip of digit may result in gangrene. 4 patients presented with gangrene of toes and fingers.

## GIT INVOLVEMENT

In this study 24 patients [48%] showed evidence of GIT involvement in form of nausea vomiting and dyspepsia. According to Hochberg et al this may represent low-grade peritoneal inflammation (or) vascular disease of bowel (or) related to medication.

Oral ulcer is seen in 38 patients [76%].

USG evidence of hepatosplenomegaly and lymphadenopathy is seen in 10 patients [20%].

2 patients presented with Acute Cholecystitis.

Eye manifestation in form of R Eye Retinal Vasculitis and CRAO is seen in 2 patients.

## Frequency of laboratory abnormalities in SLE

As far as laboratory profile is concerned following results are observed.

37 patients blood report revealed anemias [74%]. Most of them are normocytic normochromic anemias. 1 patient presented with hemolytic anemia another patient presented with recurrent anemia and fever.

**Leucopenia** generally range from 2600 cells and 4000 cells/$mm^3$ and is often associated with active disease. 5 patients had leucopenis [10%].

**Thrombocytopenia**

4 patients had thrombocytopenia [8%]. One patient presented initially with idiopathic thrombocytopenia.

**Pancytopenia**

Is seen in 3 patients.

**ESR** was found to be raised in all of the patient but with a significant rise in patients with infection disease flare and vasculitis.

Serological examination of A.N.A showed positive in all 50 patients. The patient was 70% homogenous and 30% peripheral rim pattern.

Anti ds DNA examination by farr assay revealed positive in 24 patients [48%].

Anticardiolipid andibody is associated with increased risk of seizure[63].

Frequency of laboratory abnormality in SLE of our study is compared to similar study in other parts of India[60]

| Abnormality | Northern | Sourthern | Our Study |
|---|---|---|---|
| Anaemia | 38 | 52 | 74 |
| Thrombocytopenia | 10 | 7.5 | 8 |
| Leucopenia | 16 | 12.4 | 10 |
| Non Nephrotic | 45 | 40 | 20 |
| Nephrotic | 8 | 5 | 12 |
| ANA | 98 | 96 | 100 |
| Anti ds DNA | 55 | 60 | 48 |

According to Hochberg et al ESR was found to be raised in all patients but significant rise is found in patients with disease flare and vasculitis.

According to Hochberg et al patient with mesangial nephritis have small amount of proteinuria [< 1 gm/dl]. Pt with membranous nephropathy have proteinuria often at nephritic range. Patient with proliferative nephritic have hypertension, nephritic urine sediment ,various degree of proteinuria., high titre of anti ds DNA antibodies are found in-patient with proliferative nephritis.

**Mortality and Morbidity**

Mortality was seen in 3 patients during the study.

| Lupus Nephritis | 2 Patients |
|---|---|
| Dvt/pulmonary embolism | 1 Patient |

According to one study early deaths are caused by active disease infection n and nephitis are major cause of mortality in all stages of SLE.[64]

According to Hochberg et al 10% patients of systemic lupus may demonstrate acute thromboplebitis as a feature of their illness either as a manifestation of lupus vasculitis (or) a/w cirrculating anticogulant . previous venous inflammation give rise to secondary thrombosis followed by multiple pulmonary embolism.

A Europian study of 1000 patients with SLE demonstrated 10 years survival probably of 92% reduced to 88% presented with nephropathy . mean age of death was 44 varies widely from 18.-81 years .cause of death varies . Renal lupus is the biggest number of death in those with less than 5 years of disease where as vascular disease was the most common factor who died later in the disease.[65]

# CONCLUSION

- Mean Age of SLE is 31 years.
- Highest Incidence is found in age group of 29-35 years of age.
- The most common clinical presentation in our study is muskuloskeletal involvement seen in 90%.
- Next most common presentation is skin lesions seen in 82%.
- Neuropsychiatry manifestation seen in 54%
- Renal involvement is seen in 34%
- GIT involvement is seen in 48%
- Most common initial presentation in our study is musculoskeletal involvement similar to the western data. Incidence of renal lesion as initial presentation in western data is more compared to my study.
- Normocytic nonmochromic anemias was the most common presentation leucopenia 10% ; thrombocytopenia 8% as far as haematological manfestation are concerned.
- ANA was positive in all patients.

- Anti ds DNA is seen in 48%. Anti ds DNA is seen in all patients with lupus nephrits compared to vascular lesions.

- Renal biopsy revealed active renal disease and evidence of diffuse proliferate glomerulonephrtis seen in 7 patient. Patients with DPGN have nephritic range proteinuria hypertension ds DNA. Membranous nephropathy have nephrotic range proteinuria.

- ESR raised in almost all patients with SLE. But significant increase is seen in vasculitis and active lesions.

- Death is seen in 3 patients during the course of study. 2 of them died of lupus nephritis and 1 patient died of vascular cause.

# BIBILIOGRAPHY


1. BLOTZERJW ; Systemic Lupus Erythematosus 1; Historical aspects; *Md.Med.J.* 32:439, 1983

2. Kaposi MC; Neu Beitrage Zur Keantiss des lupus erythematosus, *Arch Dermatol Syphilod* 4:36, 1872.

3. Libman E, Sacks B, A hitherto undescribed form of valvular and murla Endocarditis. *Arch. Intern. Med.* 33;701, 1924.

4. Hargraves MM, Richmond H, Morton R. Presentation of two Bone marrow Elements; That tart cell and LF cell. *Mayochn. Proc.* 23:25, 1948.

5. Frior GJ; Clinical application of Lupus Serum Nucleoprotein reaction using Fluorescent antibody technique. *J.Clin.Invest.* 36; 390, 1957

6. Deicher HR, Holman HR, Kunkol HG, The Precipitin reaction between DNA and a serum factor in SLE. *J.Exp.Med.* 109;97, 1959

7. Tan EM, KunKECHG; Characteristics of a soluble nuclear antigen precipitating with sera from patients with SLE. *J.Immunol.* 96; 464, 1966

8. Arnett FC, Shulman LF ; Studies in Familial SLE. *MEDICINE* 55:313, 1976.

9. MASI AT; Clinical Epidemilogic perspective of SLE P.145. In Lawrence RC, Shulman LE (Eds); Epidemiology of Rheumatic diseases, Gower New York 1984.

10. FESSEL WJ; Epidemiology of SLE. *Rheum.Dis.Clin. North Am.* 14:15, 1988

11. ASHERSON RA, Cervera R, Lahita RG; Latent, Incomplete (or) Lupus at all? *Rheumatology* 18: 1783, 1991.

12. Hoffman GS; Polyarthritis, The DD of RA, Semi Arthritis, *Rheum.* 8:115, 1978

13. FELDMAN DS, Zuckerman JD, Buyon JP, Articular manifestations of SLE. P.823. In Lahita RG (ed); SLE 2nd ed. Churchill Livingston, New York 1992.

14. Aseptic Necrosis of bone in SLE. Abeles M, Urman JD, Rothfield N. *Arch.Int.Med.* 138:750, 1978.

15. Isenberg D; Myositis in other connective tissue disease. *Clin.Rheumato Dis.* 10: 151, 1984.

16. Robb. Nicholson LC, Liang MH, Dalhoy L et al; Effects of acrobic conditioning in Lupus fatigue, A piton study. *J.Rheum.*28:500, 1989.

17. Stahl JI, Klippel JH, Decker JL. Fever in SLE. *Am J. Med.* 67: 933, 1979.

18. Cardinali C, Caproni M, Fabbri P. The utility of Lupus test on sun protected non leshional skin for diagnosis of systemic lupus Erythematosus. *Clin. Exp.Rhumatol* 199; 17: 427 – 432

19. Gammon RW, Briggaman RA, Inman AO. Evidence supporting a role for immune complex mediated inflammation in pathogenesis of bullous leshions of systemic lupus Erythematosus. *J. Invest Dermatol* 1983; 81 : 320 – 325

20. EMERIT, Michelson AM. Mechanism of Photosensitivity in systemic Lupus Erythematosus patients. *Proc. Natl Acad. Sci. USA* 1984; 78 : 2537 – 2540

21. APPEL GB, Silva FG, Pirani CL. Renal involvement in SLE. A study of 56 patients emphasizing histologic classification. *Med.* 57; 371, 1978.

22. Baldwin DS, Lowenstein J, Rotnfield NF. The clinical course of the proliferative and membranous forms of Lupus. *Ann. Int. Med.* 73; 929, 1970

23. Mosca M, Pasquariello A, Tavoni A, et al. Predictors of renal outcome in DPGN in SLE. 6; 371, 1997.

24. Wang C, Livy. Wang H. [Lupus Nephritis in male adults, an analysis of clinical and pathological features] Zhonghva Neike zazhi. 1995 Dec. 34[12]: 827 – 30

25. PARVEZ KHAJEHDE HI. Comparison between Males and Females with Lupus Nephritis Nephrology 3[5], 353 – 356

26. Martinez Cordero E, Riebeling Navarro CG, Lopez zopida J. Systemic lupus erythematous in children with renal and hematological manifestations. Relation to anti DNA antibodies. 1989 Jan. 46(1); 11 – 21

27. Ito M, Kugiyama Y, Omura I. Cardiovascular manifestation of SLE. *JP Circ. J.* 43: 985, 1979.

28. Stevens MB. SLE and the Cardiovascular system. *The Heart* p.707. In Lahita RG(ed); SLE 2nd Ed. Churchill Livingston NY 1992

29. Jolles PR, Tatum JL, SLE Myocarditis. Detection by Ga 67 citrate scintigraphy. *Clin. Nucl.Med.* 21; 284; 1996.

30. Rantapaa Dahlquist S, Neumann-Anderson G, Backmann C, Dahalen G, Stegma Yr B. Echocardiographic findings, lipids Lipoprotein(a) in patients with SLE. *Clin. Rheumatol.* 16; 140, 1997

31. Gabrielli F, Alcini E, Dipm, Mazzacurati G, Masala C. Cardiac valve involvement in SLE, lack of correlation with antiphospholipid antibodies. *Int.J. cardiol.* 51: 117, 1995

32. Ziporen L, Goldberg I, Aradmetal, Libman saks endocarditis in APL syndrome, immuno pathological findings in deformed heart valves. *Lupus* 5; 196, 1996.

33. Morquet AJ, Sandrock D, Stille-siegener M, Figulla HR. Indium III Antimyosin Fab imaging to demonstrate myocord involvement in SLE. *J.Nucl.Med.* 36: 1432, 1995.

34. Lagena B, Tubani L, Maffeo et al. Heart rate variability and cardiac autonomic function in SLE. *Lupus.* 5: 49, 1996

35. McCUNE WJ, Golbus J. Neuropsychiatric Lupus. *Rheum.Dis.Clin. North Am.* 149:1998

36. FEINGLASS E.J. Arnett FC, Dors. Neuropsychiatry manifestations of SLE; Diagnosis clinical spectrum and relationship to other features of the diseases. *Med.* 55: 323 – 1976

37. Kohen M, Asherson RA, Gharavi AE, Lahita RG. Lupus Psychosis, DD from the steroid induced state. *Clin. Exp. Rheumato.* 11: 323, 1993

38. Palme S, Arellano R, Meikonian E, Guzman L. Acute Abdomen due to mesenteric vasculitis as a presentation form of SLE. *Rev.Med.Clin.* 124:89, 1996

39. Wakiyama S, Yoshimara K, shimada M, Sugimachi K. Lupus peritonitis mimicking acute surgical abdomen in a patient with SLE. *Report of a case Surg. Today* 26:715, 1996

40. Bearn AG, Kunkel HG, Slater RJ. The problem of chronic liver disease in young women. *Am.J.Med.* 21:3, 1956

41. Seaman WE, Plotyz PH. Effect of Aspirin on liver tests in patients with RA/SLE and in normal volunteers. *Arthritis Rheum.* 19 155, 1976.

42. Marchesoni A, Messina K, Carrieri P. Pulmonary Hypertension and SLE. *Clin. Exp. Rheumatol.* 1:247, 1983

43. Matthay RA, Schwart MI, Petty TL. Pulmonary Manifestations of SLE. Review of twelve cases of Acute Lupus Pneumonitis. *Med.* 54: 397, 1974

44. Susanto I, Peters JI. Acute Lupus pneumonitis with normal chest radiograph. *Chest.* 111; 1781, 1997

45. Zamora MR, Warner ML, Tuder R, Schwartz MI. Diffuse alveolar haemorrhage and SLE. Clinical presentation. *Med.(Batt)* 76: 192, 1997.

46. Wilcox PG, Stein HB, Clarcke SD. Phrenic nerve function inpatients with diaphragmatic weakness and SLE. *Chest* 93: 352, 1988.

47. Buddman DR, Stein Burg AD. Hematologic aspects of SLE. Current concepts. *Ann. Int. Med.* 86: 220, 1977

48. Laurance J, Wong JEL, Nachman R. The cellular hematology of SLE. Pp 771 – 806. In Lahita RG(ed):SLE 2nd ed. Churchill Livingston NY. 1992.

49. MellenK, Jaer L, Anderson V, Linet MS et al. Non Hodgkins lymphoma and other cancers among a cohort of patients with SLE. *Arthritis Rheum.* 40: 761, 1997

50. GOLD DH, Morris DA, Honxind P. Occular findings in SLE. *Dr.J.Opthal.* 56: 800, 1972.

51. Stafford-Braddy F, Urowitz MB, Gladman DD. Lupus Retinopathy. *Arth.Rheum.* 31:1105, 1988.

52. Cunningham ETJ, Alfred DR, Trrivine AR. Central Serous Retinopathy in patients with SLE. *Opthal.* 103: 2081, 1996.

53. The Association of Physicians of India/Postgraduate Medicine Vol.18/2004.

54. Kataoka H, Takeda T, Nakatani H, Saito H, Sensoneural Hearing loss of suspected auto immuno aetiology. A report of three cases. Auris nasus larynx 22: 53, 1995.

55. Esdaile JM, Ahrahansowiez M Joseph et al; Lab Tests as predictors of disease exacerbation in SLE. Why some tests fail. Arth.Rheum. 39; 370, 1996.

56. Herbert LA, Dillon JJ, Middendroff DF, Lewis EJ, Peter JB. Relatioship between appearance of Urinary Red Blood Cell/white blood cell casts and onset of Renal relapse in SLE. Am J Kidney Dis. 26; 432, 1995.

57. Chen RY, Wong KL, Lawton JW, Hofc; ANA detection using streptavidin Biotin peroxidase complex on HEP.2 cell substrate. Asian Pac.J. Allergy immunol. 10; 19, 1992.

58. Urowitz MB, Gladmana DD, ANA negative lupus P.561. In Lahita RG (ed); SLE 2nd Ed. Churchill Livingston, New York 1992.

59. Hoffmann GS; Polyarthritis, The DD of RA; Semin Arthritis Rheum 8; 115, 1978.

60. Journal of Indian Rheumatology Association Vol.10 No.4 December 2002

61. Hochberg et al study.

62. Parviz Khajehdehi, Ghanbaralirais – Jalali ; Comparison between males and females with lupus nephritis. Nephrology 3(5), 353 – 356.

63. Predictive factor for seizure attack in patients with SLE. Park MC, Park YB. J.Korean Rheum. Association 2003 Dec. 10(4): 351 – 357.

64. Akbar Rajace, Sacid Behzadi, Shiray Z. E.Medical Journal Vol. 6 No.1 and 2 April 2005

65. Jessica J Manson and Anisor Rahman Orphanet J.Rare Dise. 2006; 1 : 6.

# PROFORMA

## PARTICULARS OF THE PATIENT

| | | |
|---|---|---|
| 1. | Name | : |
| 2. | Age | : |
| 3. | Sex | : |
| 4. | Occupation | : |
| 5. | Hospital No. | : |
| 6. | Address | : |

**Chief Complaints:**

**HISTORY OF PRESENTING COMPLAINTS:**

| | |
|---|---|
| Systemic | Y/N |
| Fatigue | Y/N |
| Malaise | Y/N |
| Fever | Y/N |
| Anorexia | Y/N |
| Weight loss | Y/N |
| Musculo Skeletal | Y/N |
| Arthalgia | Y/N |
| Myalgia | Y/N |
| Hand deformity | Y/N |
| Cutaneous | Y/N |
| Photosensitivity | Y/N |
| Malar Rash | Y/N |
| Oral Ulcers | Y/N |
| Alopecia | Y/N |

**RENAL MANIFESTATIONS:**

| | |
|---|---|
| Edema | Y/N |
| Haematuria | Y/N |

**NERVOUS SYSTEM:**

| | |
|---|---|
| Cognitive Dysfunction | Y/N |
| Memory | Y/N |
| Headache | Y/N |
| Seizure | Y/N |
| Psychosis | Y/N |
| Stroke | Y/N |

**HAEMATOLOGICAL:**

| | |
|---|---|
| Easy fatigability | Y/N |
| Lymphadenopathy | Y/N |

**CARDIAC MANIFESTATIONS:**

| | |
|---|---|
| Chest pain | Y/N |
| Palpitation | Y/N |

**PULMONARY MANIFESTATIONS:**

| | |
|---|---|
| Dyspnoea | Y/N |

**GASTROINTESTINAL MANIFESTATIONS:**

| | |
|---|---|
| Nausea | Y/N |
| Vomiting | Y/N |
| Abdominal pain | Y/N |
| Distention | Y/N |
| Obstruction | Y/N |

**PAST HISTORY:**

| | |
|---|---|
| Hypertension | Y/N |
| Diabetes Mellitus | Y/N |
| Tuberculosis | Y/N |
| Bronchial Asthma | Y/N |
| Chronic Obstructive Pulmonary Diseases | Y/N |
| Heart disease | /N |
| Kidney Disease | Y/N |
| Seizure | Y/N |
| Recurrent Abortions | Y/N |
| C.V.A. | Y/N |

**PERSONAL HISTORY:**

| | |
|---|---|
| SMOKING | Y/N |
| ALCOHOL | Y/N |
| Tobacco | Y/N |
| Premarital contact | Y/N |
| Extra marital contact | Y/N |

**FAMILY HISTORY:**

**CLINICAL EXAMINATION**

- Conscious
- Oriented
- Temperature
- Anemia
- Clubbing
- Pedal Edema
- Icterus

**Lymphadenopathy**

- Pulse **:**
- B.P. **:**
- R.R. **:**
- Cutaneous
- Malar Rash
- Oral Ulcer
- Alopecia
- Photo sensitivity Rash
- Hand deformity

**C.V.S.**

- S1
- S2
- Murmur
- Pericardial Rub

**R.S.**

- N.V.B.S.
- Added sounds
- Crackles
- Rhonchi
- Pleural rub
- Breath sound

**P/A**

- Soft
- Tenderness
- Hepatomegaly
- Splenomegaly

**C.N.S.**

FND

**INVESTIGATIONS:**

**URINE ROUTINE EXAMINATION**

- Albumin
- Sugar
- Deposits

24 hours urine protein

1. TC :
2. DC :
3. ESR :
4. Haemoglobin :
5. Peripheral Blood smear study :
6. Blood sugar :
7. Blood urea :
8. Serum Creatinine :
9. LFT :
10. RA Factor :
11. ANA :
12. Pulmonary Function Test :
13. Anti DS DNA :
14. X ray chest PA view :
15. CT Chest :
16. ECG :
17. Echo :

# ETHICAL COMMITTEE CLEARANCE

Ref.No. /ME1/2007

Stanley Medical College,
Chennai-1 Dt. -9-2007

Sub:Medical Education—Stanley Medical College, Chennai—
Ethical Committee constituted for approval of Dissertation/
Thesis submitted—regarding.

The Ethical Committee meeting was held on 3-9-2007 and 7-9-2007 to discuss the paper submitted for Dissertation /Thesis.

The following Members of the Ethical Committee were present and discuss in detail for the approval of the papers presented by the individual by means of power point presentation.

Dr.A.Sundaram, Dean incharge,
Dr.S.Madhavan, Prof. of Pharmacology,
Dr.Thenmozhivalli, Prof. of Microbiology,
Dr.S.Natarajan, Prof. of Medicine,
Dr.K.Balasubramanian, Prof. of Physiology
Dr.M.L.Shyamala, Prof. of Surgery,
Thiru M.Panneerselvam, Junior Administrative Officer.

**LIST OF PAPERS SUBMITTED FOR ETHICAL COMMITTEE APPROVAL**
ETHICAL MEETING

Dr. Kiruba Mohan, Prof. of Dermatology

1."N.O.C. for PMS study of pregabalin" - Dr.Parimalam Kumar
2. " A Phase IIb/III trial of LLL-3348 of lupin ltd in plaque psoriasis – Dr.A.Ramesh

Dr.M.Thirunavkarasu, M.D.(Psy)D.PM , Prof. of Psychiatry
"Prevalence, socio-demographic variables and method of suicide among various causes of death."

(2)Psychological autopsy of suicide.

V.Rohit
Effect of chewing gums (XYLITOL)

K.Chinthnidhi
Mycotic infections in immuno compromised and cancer patients.

Malavika Prasad
Profile of Hypertensive emergencies – A study of 100 cases from Dept. of medicine, GSH.

3. Sandhya Rani.C Final MBBS,
Assessment of coverage and quality of maternal and child health services at Minjur Primary Health Centre; Block level
4.C.Muralidharan, Final year.
The implications of mobile phones on hearing loss.
5.V.Sarath Chander, 3rd MBBS
Prevalence of Deafness in children.
6.B.Madhusoothanan, 3rd year
(1) Lung functions in type 2 diabetes.
(2)Hyponatremia in intensive medical care patients in GSH.
7.S.Sathyapriya – II MBBS.,
"A study about screening tests for cases of urinary tract infections (UTIs)Using Urine samples."
8.S.Moogaambiga,
"Estended spectrum beta lactamase producing microbes.

POST GRADUATES
1.Dr.R.Arunprakas –M1. P.G.
Analysis of clinical profile of systemic lupus erythematosus
2.Dr.S.Murugananth – M.2 P.G.
Clinical Profile of infectious fevers
3.Dr.N.Loganathan – M2 P.G.
Clinical and Epidemiological profile of Human Leptospirosis in North Chennai.
4.Dr. K. Babu – M3 – P.G.
Study of Clinical Profile of patients with acute inferior wall myocardial infarction.
5.Dr. S.P.Maharajan – M3 – P.G.
Analytical study of atrial fibrillation in Govt. Stanley Medical College Hospital.
6.Dr.P.R.Sowmini – M3 - P.G.
Clinical profile of arrhythmias complicating acute anterior wall myocardial infarction.
7.Dr.E.Uma Maheswari – M4 – PG
Clinical Radiological analysis of Focal seizures with CT Scan.
8.Dr.S.Sudha Selvi, M4 - PG
Clinical profile of chronic obstructive pulmonary disease.

9.Dr.N.Jayanthi. M6- PG
Prevalence of B2 glycoprotein 1 Dependent anticardiolipin antibodies in acute ischemic stroke.
10.Dr.Lavanya. S. – MD PG
Comparative study of fasting lipid profile in chronic renal failure patients on conservative management, on dialysis and after renal transplant.
11.Dr.R.Geetha – Pharmacology

Evaluation of the sedative effects produced by antihistamines inhealthy volunteers by new techniques.

12.Dr.K.G.Devibala, Pharmacology

To evaluate the efficacy of rupatadine in controlling pruritis in lichen planus.

13.Dr.B.Anitha, Physiology

Visual Evoked potentials in hypothyroid patients.

14.Dr.M.Thirumaran, Physiology

Heart rate variability analysis in alcohol dependant individuals.

15.Dr.K.Vinod, Anaesthesia

Real time ultra sound guided catheterization of IJV – A prospective comparison with land mark guided technique.

16.Dr.Rajesh. C.P. – M6 – PG

Cardiac conduction abnormalities and asymptomatic myocardial infarction in NIDDM patients.

The papers presented to the Committee members by the Profs./Asst. Prof./Post Graduates/Under graduates were discussed across the table while their presentation.

The above papers discussed in detail with its supportive documents submitted by them and approved the above papers submitted for Ethical Committee.

| Name of the Members | Signature |
|---|---|
| Dr.A.Sundaram, Dean incharge, | |
| Dr.S.Madhavan, Prof. of Pharmacology, | 8/10/07. |
| Dr.Thenmozhivalli, Prof. of Microbiology, | |
| Dr.S.Natarajan, Prof. of Medicine, | 9.10.2007. |
| Dr.K.Balasubramanian, Prof. of Physiology, | |
| Dr.M.L.Shyamala, Prof. of Surgery, | 08/10/07. |
| Thiru M.Panneerselvam, Junior Administrative Officer. | |